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**TITLE**

COMBINED CAFFEINE AND EPHEDRINE INGESTION IMPROVES RUN TIMES OF CANADIAN FORCES WARRIOR TEST

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# Combined Caffeine and Ephedrine Ingestion Improves Run Times of Canadian Forces Warrior Test

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The ingestion of a combination of caffeine (C) and ephedrine (E) has been reported to prolong exercise time to exhaustion during cycle ergometry at 85% $\dot{V}O_{2max}$. The present study was undertaken to investigate whether this enhancement would occur in a field setting and if drug ingestion on 1 d would affect performance 1 d later. Two hours after ingesting either a combination of 375 mg of C and 75 mg E (C+E), or a placebo (P), 9 healthy male recreational runners completed six balanced and double-blind trials of the Canadian Forces Warrior Test (WT), a 3.2 km run wearing "fighting order" which weighed about 11 kg. The trials were performed in sets of two runs, i.e., two runs were done 24 h apart, and these sets were separated by a minimum of 7 d. The sets were: C+E trial on day 1 (D1), placebo on day 2 (P2); placebo first (P1), C+E second (D2); and placebo first (P3), placebo second (P4). In addition, 1 wk before the treatment trials the subjects performed a control trial WT. During the WT, heart rates (HR) were recorded every minute. Plasma C and E levels immediately before the WT were similar for both C+E trials, but were undetectable for all P trials. Run times (mean ± SD) were 15.3 ± 0.6, 15.4 ± 0.9, 15.5 ± 1.2, 15.4 ± 0.9, 15.4 ± 0.9, 14.8 ± 0.7, and 14.6 ± 0.8 min for control, P1, P2, P3, P4, D1, D2 trials, respectively. The two C+E trial run times were similar and both were significantly faster ($p < 0.05$) than control and all placebo trials. HR during the WT was significantly higher ($p < 0.05$) for the C+E trials compared with the other trials. WT performance was not impaired by C+E ingestion 24 h earlier. In conclusion, performance of the WT was improved by ingestion of C+E.

Keywords: ergogenic aids, methyl xanthines, aerobic exercise, $\dot{V}O_{2max}$, physical fitness.

BY VIRTUE OF THEIR purported ergogenic properties, the use of either caffeine (C) or ephedrine (E) is banned by the International Olympic Committee. The former has repeatedly been shown to enhance performance (3,6,9,13,18) while the performance enhancement properties of the latter remain suspect (2,8,16). The purported mechanism of action by which C and E could enhance physical performance is through stimulation of both central nervous system (CNS) receptors and metabolic receptors in peripheral tissues including skeletal muscle (4,10,12,14,15).

The ingestion of the drugs in combination (C+E) has been the focus of obesity studies because of the resultant increased metabolic rate (1,4). Study of the effects of ingesting C+E on exercise performance is a relatively new area of investigation. We recently reported that C+E ingestion prolonged time to exhaustion during cycle exercise at an intensity of 85% of maximal aerobic power ($\dot{V}O_{2max}$) (2). The observed performance enhancement in that study was significantly greater with the combination of C+E than was the case when pretreatment consisted of ingesting either C or E alone. The present study was undertaken to test the ergogenic properties of C+E using a field test of physical performance that is relevant to military operations.

The performance test used in this investigation is called the Canadian Forces (CF) Warrior Test (WT), which is a 3.2 km run wearing "fighting order" (FO). The FO of a CF rifleman includes: helmet, rifle, webbing (i.e., straps to which back pack and canteen are attached), full canteen, a back pack, and combat boots. The total weight carried is approximately 11 kg. The WT is a standard test that all land forces combat soldiers must perform within 22 min. Thus, one purpose of this study was to determine if ingestion of C+E would improve WT performance times. It was hypothesized that C+E treatment would result in improved performance of this field test.

It was reported anecdotally by several subjects in our previous studies that they felt more fatigued and lethargic than usual after the stimulatory effects of the C+E treatment had subsided. Thus, an additional objective of this study was to evaluate the effects of C+E on performance 24 h after treatment. It was hypothesized that performance would be impaired 24 h after drug ingestion.

## METHODS

### *Subjects*

Nine male subjects with mean ± SD values for age 37 ± 10 yr, height 1.75 ± 0.05 m and weight 80.9 ± 11

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kg participated in this study. All subjects were recreational runners with peak treadmill $\dot{V}O_{2max}$ of 58 ± 5 ml · kg$^{-1}$ · min$^{-1}$. Runners were recruited in order to use subjects who would be familiar with running on two consecutive days. The subjects were fully informed of the details, discomforts and risks associated with the experimental protocol, and written informed consent was obtained.

*Procedures*

The subjects visited the laboratory on nine occasions. During Visit 1, the subjects were medically screened and then proceeded to the exercise laboratory where they performed a continuous, progressive treadmill run to exhaustion while dressed in the CF FO. During this run oxygen consumption ($\dot{V}O_2$) and heart rate (HR) was recorded every minute. Individual $\dot{V}O_2$-HR regression equations were generated for each subject which were used later to estimate the relative intensity of the field runs.

During Visits 2 and 3, the subjects were familiarized with the WT. After putting on the HR monitors and exercise clothing (T-shirt, shorts, socks and running shoes), they were fitted with the FO. The subject then performed the WT as quickly as possible over a marked, 3.2–km circular route on pavement. These two trials were separated by a minimum of 48 h. The WT run time on Visit 3 was considered as the control trial value.

During visits 4–9 the three treatment trials were conducted. Each trial consisted of a set of two runs, separated by 24 h. The three sets of two runs were separated from each other by a week and were separated from Visit 3 by a week. The sets were as follows: C+E on the first day followed by a placebo (PL) day; a PL first day followed by a C+E day; and a PL day first followed by another PL day. All treatments were carried out in a double-blind fashion. The order of the sets of runs was balanced among the subjects.

The subjects were instructed to refrain from consuming substances containing caffeine from 6:00 p.m. on the night before the treatment trials, and they reported to the laboratory in a 12–h fasted state. Then, in the presence of a technician, they ingested gelatin capsules containing either the placebo (dietary fiber, Metamucil®) or the experimental treatment consisting of 375 mg of anhydrous caffeine plus 75 mg ephedrine hydrochloride. Since this investigation was designed to evaluate the feasibility of exploiting C+E in a military operational environment, it was decided not to titrate the C+E relative to body weight because it is unlikely that C+E would ever be dispensed to a military population in anything other than an absolute dose. For reference purposes, in our previous investigation (2) C+E was used in a dose of 5 mg · kg$^{-1}$ body weight of C in combination with 1 mg · kg$^{-1}$ of E; the subjects weighed 81.4 kg.

Some 45 min after ingesting the capsules, the subjects were fed a standardized meal consisting of toast, muffin and fruit juice. Some 75 min after the meal, they reported back to the laboratory and a 5–ml blood sample was taken from an antecubital vein and subsequently analyzed for plasma caffeine and ephedrine concentration. They then donned the FO clothing and equipment and the HR monitors, and left the laboratory to perform a "best effort" WT.

Some 2 wk after the last set of runs all but one subject returned to the laboratory on two more occasions for determination of their $\dot{V}O_{2max}$ during exhaustive treadmill running after both placebo and C+E treatment. These two tests were separated by a minimum of 48 h. During these sessions the subjects wore normal exercise clothing, not FO. Procedures for these runs were as follows: 4 min of seated rest, followed by consecutive 4 min intervals of running at 9.6, 10.7, 12.0 km · h$^{-1}$ at 0% grade, followed without a break by a 1% change in treadmill slope every minute until exhaustion. The highest $\dot{V}O_2$ measured during exercise was considered as $\dot{V}O_{2max}$.

*Measurements*

During the treadmill runs, $\dot{V}O_2$, $\dot{V}O_{2max}$, and $\dot{V}_E$ were measured with an automated metabolic cart system (OCM-2 AMETEK, Pittsburgh, PA). HR during the treadmill runs and the WT trials was recorded continuously (Vantage XL Polar System, Port Washington, NY). Plasma from the venous blood samples was assayed for both caffeine and ephedrine concentration by gas chromatograph-mass spectrometry electron impact single ion monitoring (model MSD 5970a, Hewlett Packard, Palo Alto, CA). Dry bulb, wet bulb, and globe temperature were measured every day throughout the trials with a heat stress monitor (RSS-220 Reuter Stokes, Cambridge, Ontario, Canada). Relative humidity was determined from the dry bulb and wet bulb temperatures. Wind velocity was also measured every day throughout the trials with a wind anemometer (Anemometer Airflow Development, High, Wycombe, UK).

*Statistics*

A one-way repeated measures analysis of variance (ANOVA) was used to compare the WT run times and the ambient conditions across treatment trials. For all other variables a two-way repeated measures ANOVA was used to compare the dependent variables across treatments and time (7). When the ANOVA yielded a statistically significant F-ratio then a post hoc comparison of means was done with a means comparison contrast technique (7); Huyn-Feldt epsilon factors were used to adjust degrees of freedom for multiple comparisons. Statistical significance was accepted at the $p \leq 0.05$ level. A Fisher's F test was used to compare the placebo and C+E regression equations of HR vs. $\dot{V}O_2$ from the data collected during the treadmill runs. Further, the slopes and intercepts of the individual regressions were compared with a paired *t*-test. The reproducibility of the WT was assessed by plotting the results from the placebo treatment trials, calculating the regression equation and using a *t*-test to determine if the intercept of the regression equations was significantly different from zero.

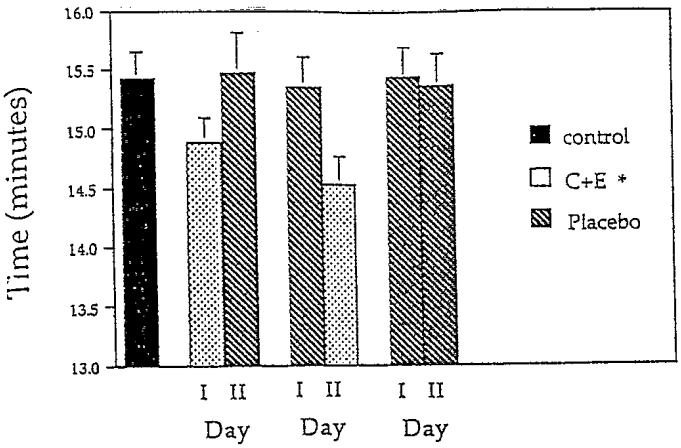


Fig. 1. Mean (±SEM) time to complete the Warrior Test. * C+E trials significantly different from control and placebo trials.

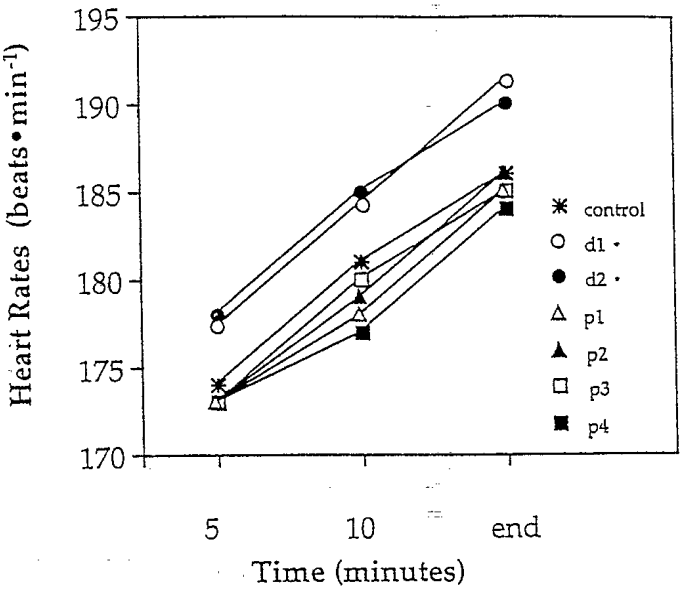


Fig. 2. Mean heart rates during Warrior Test. * C+E trials significantly different from control and placebo trials. d1, d2 = C+E trials; p1, p2, p3, p4 = placebo trials; control = control trial.

## RESULTS

The plasma caffeine levels (mean ± SD) just prior to the WT were similar for the two trials when C+E was ingested (48.8 ± 12.4 and 54.7 ± 12.0 $\mu$mol · $L^{-1}$). Plasma ephedrine levels prior to the WT were also similar during these two trials (0.430 ± 0.133 and 0.363 ± 0.103 $\mu$mol · $L^{-1}$). No caffeine or ephedrine was detectable in the plasma during the PL trials. This latter observation is important as it indicates that 24 h after C+E ingestion C and E were eliminated from the blood stream.

The ambient conditions (mean ± SD): dry bulb (22.8°C ± 3.1), wet bulb (19.4°C ± 2.0), globe temperature (33.1°C ± 6.1), relative humidity (69% ± 10) and wind velocity (2.4 m · $s^{-1}$ ± 1.7) were not significantly different among the trials and did not effect WT.

The reproducibility of the WT run times was assessed by plotting the results of the two placebo treatment trials. The resulting regression equation was $y = 1.047 + 0.936 \times$ with a correlation coefficient of 0.894 ($p < 0.05$). The intercept of the regression equation was not significantly different from zero. Also, a paired *t*-test indicated that the trials were not different.

Fig. 1 shows that the times for all the PL and control runs were similar, regardless of whether the PL treatment occurred on the first or second day of the set. The ANOVA showed that there was no difference among trials for the set of runs consisting of two consecutive PL days. Compared with the PL treatments and control, WT time was significantly improved by ingestion of C+E, regardless of whether it was ingested on the first or second day of the set. There was no difference in WT times between the two C+E trials.

Fig. 2 shows that HR increased during the WT and was significantly higher during the C+E trials compared with the control or PL trials.

Fig. 3 shows the relationship between the grouped HR and $\dot{V}O_2$ during exercise on the treadmill after PL and C+E treatments. There was no difference between the two calculated regression lines. Fig. 4 shows the $\dot{V}O_2$ at standard running velocities during the treadmill runs for the PL and C+E trials; C+E did not change the $\dot{V}O_2$. Further, during the treadmill runs $\dot{V}O_{2max}$ was similar for both the PL and C+E trials. Fig. 5 shows the HR at standard running velocities during the treadmill runs after either control or C+E treatment; C+E caused significantly higher HR.

Contrasting with our earlier trials where several subjects were nauseous during exercise in the laboratory after C+E treatment (2), no nausea or vomiting occurred during any of the trials in this investigation.

## DISCUSSION

The major finding in this study was that the 3.2–km run time was significantly improved after C+E treatment. These results extend to a field setting earlier

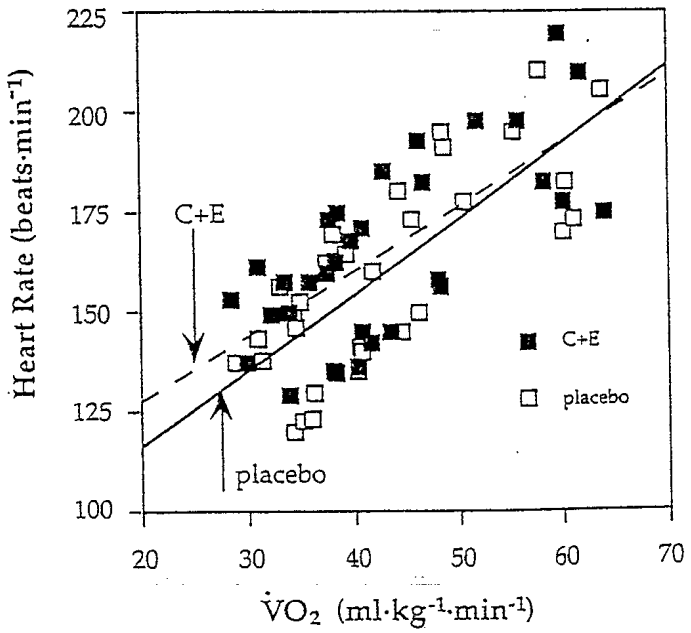


Fig. 3. Mean heart rate and oxygen uptake relationship during treadmill exercise while on and off the combination of C+E. (y = 1.9X + 77.8 placebo; y = 1.6X + 95.2 C+E).

findings that C+E treatment increased time to exhaustion during cycle ergometer exercise at 85% $\dot{V}O_{2max}$ (2). The improvement in the 3.2-km run time, from a mean value of 15.4 min for the PL trials to 14.7 min for the C+E trials, is particularly significant given the estimated intensity of exertion during the runs, which probably exceeded 90% $\dot{V}O_{2max}$ based on the HR recordings.

Caffeine in particular has well established potent metabolic effects on energy metabolism during moderate intensity submaximal exercise, but the effects on such high intensity exercise are equivocal (14,17). Our earlier investigation (2) demonstrated that during such high intensity exercise the magnitude of the performance enhancement caused by the combination of C+E exceeded that caused by the administration of a similar dose of caffeine alone. The findings were attributed to increased central nervous system stimulation (2). This conclusion was supported by the observation of lower subjective ratings of perceived exertion after C+E treatment (2); in the absence of differences in either $\dot{V}O_{2max}$ or submaximal $\dot{V}O_2$, lower perceived exertion would suggest that the C+E was having an effect that was more centrally mediated. Such an effect would help explain the current results because it is consistent with the interpretation that C+E enabled the subjects to exercise at a higher percentage of the maximal aerobic power for a longer period of time, compared with the PL trials.

The faster running velocity for the WT was associated with a higher HR during the C+E trial. HR was also higher for the C+E trials during the treadmill runs at oxygen uptakes that were identical to the PL trials. Maximal HR both during the treadmill runs and the WT was also higher for the C+E trials than the PL trials. Taken together, these observations suggest that the improved performance was in large measure due to the well established general CNS stimulatory effects of both caffeine and ephedrine, mediated by both monoamine and serotonin receptors (10,15). The data suggest that the relationship between the perception of effort and heart rate response appears to have changed as a result of the ingestion of C+E.

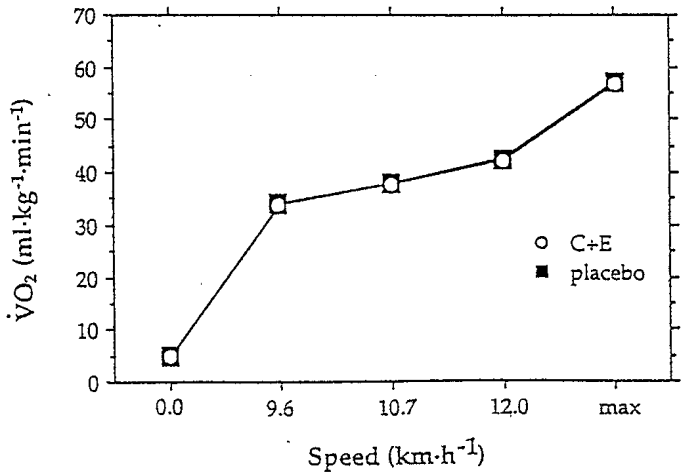


Fig. 4. Mean (±SEM) $\dot{V}O_2$ during rest, submaximal exercise and maximal exercise while on and off the combination of C+E. Note that the C+E values overlap the placebo values and the SEM bars fall within the legend symbols.

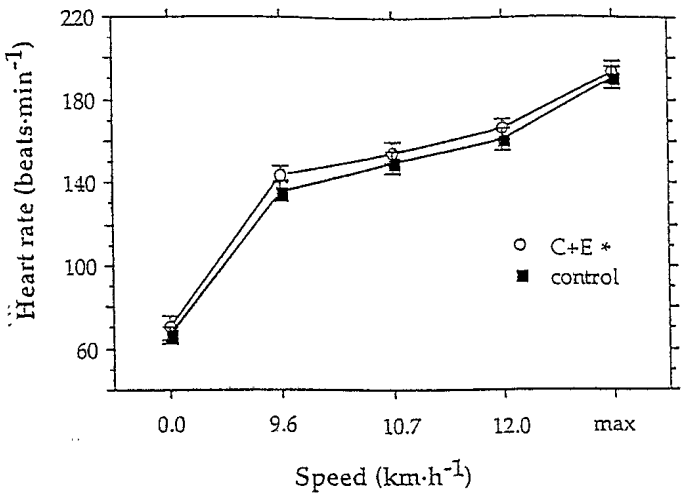


Fig. 5. Mean (±SEM) heart rate during rest, submaximal exercise and maximal exercise while on and off the combination of C+E. * C+E trials significantly different from control trial.

Regarding our secondary hypothesis, there were anecdotal reports by subjects in previous investigations that they felt unusually lethargic for 24 h after C+E treatment. This led to our secondary hypothesis that exercise performance 24 h later would be impaired, but the present results did not support this hypothesis.

In conclusion, the ingestion of a combination of caffeine and ephedrine induced an acute improvement in the performance of a military field test which involved running a 3.2-km course while carrying a light load. This treatment did not cause performance impairments 24 h later.

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